JACC Vol. 22, No. 1
July 1993:135–43

Multicenter Investigation of Coronary Stenting to Treat Acute or Threatened Closure After Percutaneous Transluminal Coronary Angioplasty: Clinical and Angiographic Outcomes

BARRY S. GEORGE, MD, FACC, WILLIAM D. VOORHEES III, PHD,*
GARY S. ROUBIN, MBBS, PHD, FACC, NEAL E. FEARNOT, PHD, CASS A. PINKERTON, MD, FACC,
ALBERT E. RAIZNER, MD, FACC, SPENCER B. KING, MD, FACC, DAVID R. HOLMES, MD, FACC,
ERIC J. TOPOL, MD, FACC, DEAN J. KEREIAKES, MD, FACC,
GEOFFREY O. HARTZLER, MD, FACC
Columbus, Ohio and West Lafayette, Indiana

Objectives. **This study reports on the initial experience with the Gianturco-Roubin flexible coronary stent. The immediate and 6-month efficacy of the device and the incidence of the complications of death, myocardial infarction, emergency coronary artery bypass surgery and recurrent ischemic events are presented.**

Background. **Abrupt or threatened vessel closure after coronary angioplasty is associated with increased risk of myocardial infarction, emergency coronary artery bypass graft surgery and in-hospital death. When dissection or prolapse of dilated plaque into the lumen is unresponsive to additional or prolonged balloon catheter inflation, coronary stenting offers a nonsurgical mechanical means to rapidly restore stable vessel geometry and adequate coronary blood flow.**

Methods. **From September 1988 through June 1991, 518 patients underwent attempted coronary stenting with the 20-mm long Gianturco-Roubin coronary stent for acute or threatened vessel closure after angioplasty. In 494 patients, one or more stents were deployed. Thirty-two percent of patients received stents for acute closure and 69% for threatened closure.**

Results. **Successful deployment was achieved in 95.4% of patients. Overall, stenting resulted in an immediate angiographic improvement in the diameter stenosis from 63 ± 25% before stenting to 15 ± 14% after stenting. Emergency coronary artery bypass graft surgery was required in 4.3% (21 of 493 patients). The incidence of in-hospital myocardial infarction (Q wave and non-Q wave) was 5.5% (27 of 493 patients). At 6 months, myocardial infarction was infrequent, occurring in 1.6% (8 of 493 patients). The incidence of in-hospital death was 2.2% (11 of 493 patients). Late death occurred in 7 patients (1.4%) and 34 patients (6.9%) required later bypass graft surgery. Complications included blood loss, primarily from the arterial access site, and subacute thrombosis of the stented vessel in 43 patients (8.7%).**

Conclusions. **The early multicenter experience suggests that this stent is a useful adjunct to coronary angioplasty to prevent or minimize complications associated with flow-limiting coronary artery dissections previously correctable only by surgery. Although this study was not randomized, it demonstrated a high technical success rate and encouraging results with respect to the low incidence of emergency coronary artery bypass graft surgery and myocardial infarction.**

(J Am Coll Cardiol 1993;22:135–43)

Acute coronary artery dissection causes unpredictable abrupt vessel closure and ischemia during percutaneous transluminal coronary angioplasty. Despite continued improvements in equipment and the technical aspects of the procedure, abrupt vessel closure still occurs in approximately 2% to 10% of all patients undergoing coronary angioplasty (1). In the 1985–1986 National Heart, Lung and Blood Institute Percutaneous Transluminal Coronary Angioplasty Registry, its incidence was 6.8%; in these patients, 32% required emergency coronary artery bypass surgery, 42% had in-hospital myocardial infarction and 5% died before hospital discharge. By 6 months, 45.9% of these patients had bypass surgery, 41% had myocardial infarction and 6.6% died. Similar rates of adverse events have been reported by several other investigators (2–4) for similar groups of patients.

Intracoronary stents with a variety of designs have been developed to treat dissections or acute closure after angioplasty (5–7). By providing a prosthetic intraarterial scaffold, the stent can correct the geometric limitations to coronary blood flow not uncommonly seen after angioplasty-induced coronary artery dissection. The Gianturco-Roubin flexible coronary stent (Gianturco-Roubin Flex-Stent, Cook Inc.)

From the Mid-Ohio Cardiology Research Foundation, Riverside Methodist Hospital, Columbus, Ohio and *MED Institute, Inc., West Lafayette, Indiana. A complete list of participating centers appears in the Appendix. This study was supported in part by funding from Cook Incorporated, Bloomington, Indiana.

Manuscript received August 7, 1992; revised manuscript received November 4, 1992, accepted December 1, 1992.

Address for correspondence: Barry S. George, MD, Midwest Cardiology Research Foundation, 3400 Olentangy River Road, Columbus, Ohio 43214.

0735-1097/93/$6.00

JACC Vol. 22, No. 1
July 1993:135–43

has been under laboratory and clinical investigation since 1985 (8–15). In May 1992, the Circulatory System Devices Advisory Panel of the Food and Drug Administration recommended commercial approval of this device to treat acute or threatened vessel closure. The purpose of this study is to report the early multicenter experience with this stent. The immediate and 6-month efficacy of the device and the incidence of the complications of death, myocardial infarction, emergency coronary artery bypass surgery and recurrent ischemic events are presented.

Methods

Study patients. From September 1988 through June 1991, 518 patients were enrolled in a multicenter clinical trial of the 20-mm long balloon-expandable flexible Gianturco-Roubin coronary stent at 19 investigative centers throughout the United States (see Appendix). The indication for stenting was acute or threatened vessel closure complicating a conventional coronary angioplasty procedure. Four hundred ninety-four of these patients had one or more coronary stents implanted. All patients gave written informed consent for implantation of the investigational device. The study protocol was approved by the Institutional Review Board of each investigative center.

Definitions. *Acute vessel closure*, defined as occlusion of a vessel with Thrombolysis in Myocardial Infarction trial (TIMI) grade 1 or 0 flow, was based on the angiographic appearance of the vessel immediately before stent insertion. *Threatened vessel closure* was defined as deterioration in arteriographic, electrocardiographic (ECG), hemodynamic or clinical indicators after coronary angioplasty and required at least two of the following criteria: 1) postangioplasty residual stenosis ≥50%, 2) TIMI grade 2 flow, 3) significant dissection, or 4) clinical evidence of ischemia (that is, typical angina or ECG changes).

Immediate angiographic success of the angioplasty/stent procedure was defined as reduction of diameter stenosis by ≥20% and a residual diameter stenosis <50% after the procedure. *Angiographic restenosis* was defined as >50% diameter narrowing at the stent site at any angiographic follow-up study. Stenosis diameter was measured with electronic digital calipers. Measurements were taken from the angiographic view that showed the lesion most clearly and with the most severe narrowing.

In-hospital clinical success was defined as immediate angiographic success with no major ischemic complication (myocardial infarction, bypass surgery or death).

Myocardial infarction was defined as the development of new pathologic Q waves (≥40 ms) or elevation of creatine kinase to more than twice the normal upper limit with an elevated creatine kinase-MB fraction after stent placement, or both.

Percutaneous transluminal coronary angioplasty procedure. Coronary angioplasty was performed using conventional techniques. The preangioplasty medical regimen evolved during the course of the trial. Most patients received either diltiazem or nifedipine the night before the procedure and soluble aspirin and dipyridamole on the morning of the procedure. On the basis of the findings of earlier feasibility trials, stent thrombosis was observed to be minimized with the use of soluble aspirin, rather than enteric-coated aspirin, plus dipyridamole (75 mg orally, three times daily). At least two 325-mg doses of soluble aspirin were regularly given (one dose on the morning of the procedure). Patients with lesions determined to be at high risk for acute closure were often pretreated with dextran 40, 10% solution, at 50 to 75 ml/h for ≥2 h before the angioplasty procedure. Intraarterial heparin (10,000 to 15,000 U) was given at the start of the procedure and supplemented as needed to achieve a target activated clotting time of ≥300 s.

The coronary angioplasty procedure was performed using standard techniques at each institution. If acute closure of the artery or an unstable angiographic appearance developed during the course of the procedure, patients were generally further treated with prolonged inflations with either the same balloon or with a balloon 0.5 mm larger. At the discretion of the operator, a perfusion balloon system was employed. When appropriate, the patient proceeded directly to stent implantation.

Once the decision to stent the lesion was made, a bolus dose (100 to 200 ml) of dextran 40, 10% solution, was given intravenously and the infusion continued at 100 ml/h for 2 h then at 50 ml/h until the sheaths were removed and a therapeutic infusion of heparin was reestablished.

Stenting procedure. The Gianturco-Roubin flexible coronary stent has been described in detail previously (8). Briefly, this stent is composed of a continuous single strand of 0.006-in. (0.15 cm) diameter surgical grade stainless steel wire. The wire is formed into a cylinder of interdigitating loops (Fig. 1). This design provides high hoop strength and ensures that stents will not shorten with radial expansion. The stents used in this study have an effective length of 20 mm. Stents are supplied in nominal expanded diameters of 2, 2.5, 3, 3.5 and 4 mm. Each stent is supplied tightly prewrapped around a polyethylene compliant balloon catheter. The balloons are 30 mm long and have nominal inflated diameters 0.5 mm larger than the nominal expanded diameter of the stent.

The deflated balloon/stent catheter is relatively flexible and can be positioned at the target site by a slightly modified over the wire technique. The profile of the stent/balloon catheter requires large lumen 8F guiding catheters for the 2-, 2.5- and 3-mm stents and large lumen 9F guiding catheters for the 3.5- and 4-mm stents. Moreover, the selected guiding catheter must provide optimal backup support. Trackability of the device is enhanced by using 0.018-in. (0.045 cm) coronary guide wires. The stent/balloon catheter was carefully advanced to the lesion and the balloon was inflated to 5 to 8 atm depending on the stent diameter. After complete balloon deflation was ensured, the balloon catheter was gently advanced approximately 1 mm to disengage the stent,

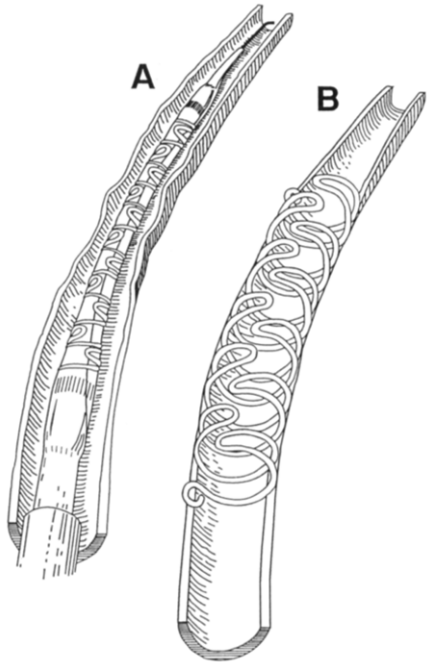

Figure 1. Diagrams showing the stent before and after balloon inflation. The stent is composed of a single strand of surgical grade stainless steel wire formed into a cylinder of interdigitating loops. This design provides high hoop strength and ensures that the stent will not shorten when expanded. **A,** The stent is wrapped tightly around the delivery balloon before inflation. **B,** The balloon is inflated, then thoroughly deflated and disengaged leaving the expanded stent in place. Redrawn, with permission, from Garratt et al. (12).

then withdrawn leaving the expanded stent in place. Angiography was repeated and further inflations were performed inside the stent if necessary to produce an optimal lumen result. If the balloon could not be advanced to the desired position, the stent was removed by withdrawing it to the tip of the guiding catheter and removing the stent/balloon catheter and the guiding catheter as a unit through the arterial sheath. At the end of the procedure, catheters were removed, sheaths were left in place and the patient was taken to the coronary care or angioplasty nursing unit. An ECG was recorded immediately after angioplasty and daily for 2 days. Creatine kinase and isoenzyme estimations were performed immediately and every 8 h for 24 h.

In patients with angiographic evidence of intracoronary thrombus, an intracoronary urokinase infusion was administered. After the procedure, administration of heparin was discontinued or decreased until the activated clotting time was ≤150 s and the sheaths removed. Early in the study, the sheaths were left in and the heparin infusion was continued until the next day. Later in the study, sheaths were removed at 4 to 6 h after the procedure when the activated clotting time had decreased to ≤150 s. Pressure was maintained on the groin for 1 h, at which time the heparin infusion was restarted. Titration with Coumadin (warfarin) was initiated. Heparin administration was continued until the prothrombin time was >17 s on two blood samples taken 12 h apart. Dextran infusion was continued until the partial thromboplastin time was within the therapeutic range (50 to 80 s) after sheath removal. Patients continued to receive aspirin, dipyridamole and a calcium channel blocker.

Early in the study, patients were mobilized according to routine postangioplasty protocol. Approximately halfway into the study period, the mobilization protocol was modified to reduce the incidence of complications at the arterial access site in the groin. Patients lay flat in bed for the 1st 24 h after sheath removal. They were permitted to sit up in bed for the next 24 h. On the 3rd postprocedural day, patients were allowed to sit out of bed. Patients were able to walk freely in their rooms on day 4 and were discharged after stable anticoagulation with Coumadin was established. Dipyridamole and Coumadin were continued for 2 months after discharge to maintain a target prothrombin time between 17 and 22 s. Aspirin was continued indefinitely at a dosage of 325 mg/day.

Data collection. Limited patient history, details of the initial angioplasty procedure, indication for stenting and results of the stenting procedure were recorded on standard forms by a research coordinator in collaboration with the attending cardiologist. Clinical and laboratory results, including ECG changes, the presence of angina and any procedural complication, were routinely collected during the admission and reported on standard forms. Other relevant information was collected from the medical record. Clinical sites were audited to determine the accuracy of information submitted to the data coordinating center (MED Institute, Inc.).

All procedural angiograms were reviewed. Information recorded included an initial morphologic description of the lesion, TIMI grade flow and the presence or absence of dissection after angioplasty. Measurement of the stenosis was made before angioplasty, immediately after angioplasty, before stenting and within 30 min after stenting. Patients were classified according to the definition of acute or threatened vessel closure by the operator, depending on the events preceding the decision to stent. All acute closures were complete occlusions. However, the quantitative measurements were taken from the cineangiogram most closely preceding stent placement. A cineangiogram of the complete occlusion event was not always available. Therefore, the average diameter stenosis reported for the acute closure group was <100%.

All patients receiving stents were requested to return for angiographic follow-up examination at 6 months. Some patients underwent angiography earlier for clinical evaluation or because of the recurrence of symptoms. At follow-up, cineangiograms were taken in views as similar as possible to those used during the initial procedure.

Statistical analysis. Comparison of proportions utilizing the z test (at $\alpha = 0.05$ level of significance) was used to evaluate the difference in the incidence of adverse events between the group of patients who underwent stenting for acute closure and the group treated for threatened closure. Chi-square analysis was employed to evaluate the influence

JACC Vol. 22, No. 1
July 1993:135–43

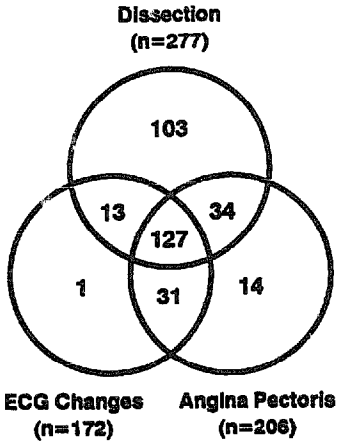

Figure 2. Schematic representation of the patients who underwent stenting for threatened vessel closure stratified according to the presence of dissection, angina pectoris or electrocardiographic (ECG) changes before stent placement.

of stent diameter and the implantation of multiple stents on the incidence of thrombosis and restenosis of the stented artery.

Results

Study patients. Stent placement was attempted in 518 patients. One or more stents were implanted in a single procedure in 494 patients (95.4%). Twelve of these patients received stents during each of two separate procedures. There were 349 men and 145 women. The mean age was 59 ± 11 years (range 27 to 85) with 171 (34.6%) aged ≥65 years. Multivessel disease was reported in 275 patients (55.7%). The initial coronary angioplasty procedure was performed as an elective procedure in 273 patients (55.2%) and under conditions of unstable angina in 157 (31.8%). Thirty-seven patients (7.5%) were reported with evolving myocardial infarction before angioplasty. Data on left ventricular ejection fraction (mean value 53 ± 11%) were available for 372 patients (75.3%).

The indication for stent implantation was acute vessel closure in 156 patients (31.6%) and threatened closure in 337 patients (68.2%). Of those patients receiving a stent for threatened closure, dissection was reported in 277 (82.2%) before stent implantation and either dissection, angina or ECG changes were present in 323 (95.8%) (Fig. 2).

Lesion and stent characteristics. The majority of stents (92.8%) were implanted in native vessels (Table 1). A broad representation of left anterior descending (36.3%), right coronary (36.3%) and left circumflex (19%) arteries were stented. Similarly, the series includes a cross section of anatomic and morphologic characteristics, including chronic occlusions (12.8%), long stenoses >15 mm (17.9%), severely tortuous lesions (8.1%), branch point stenoses (22.9%) and lesions with visible thrombus before stenting (28.1%). Nominal normal vessel diameter was <3 mm for 38.4% of the

Table 1. Distribution of the Diameters of Stents Used and the Vessels in Which They Were Implanted

	Stent Diameter (mm)					
Vessel	2	2.5	3	3.5	4	Total
LAD	17	79	83	21	1	201
RCA	2	49	102	36	12	201
LCx	1	51	46	6	1	105
LMCA	0	3	3	1	0	7
Graft to RCA	0	4	3	3	6	16
Graft to LCx	0	2	3	6	3	14
Graft to LAD	0	1	1	4	4	10
Total	20	189	241	77	27	554

LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LMCA = left main coronary artery; RCA = right coronary artery.

vessels stented. Of the stents placed, 37.7% were 2 or 2.5 mm in diameter, 43.5% were 3 mm in diameter and 18.8% were 3.5 or 4 mm in diameter. Thirty-six patients (7.3%) had stents placed in grafts. Four of these 36 patients had two stents placed in the same graft. Fifty-two patients received two stents during either a single procedure or during two different procedures and five patients received three stents. Table 2 summarizes data from the patients receiving multiple stents and the vessels stented.

Angiographic success of stenting. Four hundred ninety-four (95.4%) of 518 patients received stents. Four hundred eighty-one (97.3%) of the 494 patients with a stent met the definition for immediate angiographic success of the angioplasty/stenting procedure. Stenting resulted in an immediate angiographic improvement in the diameter stenosis from

Table 2. Summary of Patients Receiving Multiple Stents and the Vessels Stented

	No. of Patients Receiving Two Stents	
Vessels Stented	Same Procedure	Two Procedures
RCA/RCA	20*	1
LAD/LAD	10	1
LCx/LCx	4	2
LAD/LCx	2	3
RCA/LAD		3
LMCA/LMCA		1
Graft, RCA/graft, RCA	2	
Graft, LCx/graft, LCx	1	
Graft, LAD/graft, LAD	1	
Graft, RCA/RCA	1	
Total patients	41	11
	No. of Patients Receiving Three Stents	
	Same Procedure	Two Procedures
RCA/RCA/RCA	1	1*
LAD/LAD/LAD	1	
LCx/LCx/LCx	2	
Total patients	4	1*

*One patient received two stents in his first procedure and a third stent in a second procedure. Abbreviations as in Table 1.

Table 3. Incidence of Death, Coronary Artery Bypass Surgery and Myocardial Infarction During the In-Hospital Period After Stent Placement and After Discharge Within the 1st 6 Months After Stent Placement

	Vessel Closure						
	Acute (n = 156)		Threatened (n = 337)		Total (n = 493)		p
	No.	%	No.	%	No.	%	Value*
A. In-Hospital Events							
Death	4	2.6	7	2.1	11	2.2	0.983
Bypass surgery							
Emergency	12	7.7	9	2.7	21	4.3	0.021
Nonemergency	8	5.1	7	2.1	15	3.0	0.128
Myocardial infarction							
Q wave	6	3.8	9	2.7	15	3.0	0.705
Non-Q wave	6	3.8	6	1.8	12	2.5	0.305
B. Events After Discharge							
Death	3	1.9	4	1.2	7	1.4	0.840
Bypass surgery	6	3.8	28	8.3	34	6.9	0.100
Myocardial infarction							
Q wave	2	1.3	2	0.6	4	0.8	0.791
Non-Q wave	1	0.6	3	0.9	4	0.8	0.845

*Comparing the groups with acute and threatened vessel closure.

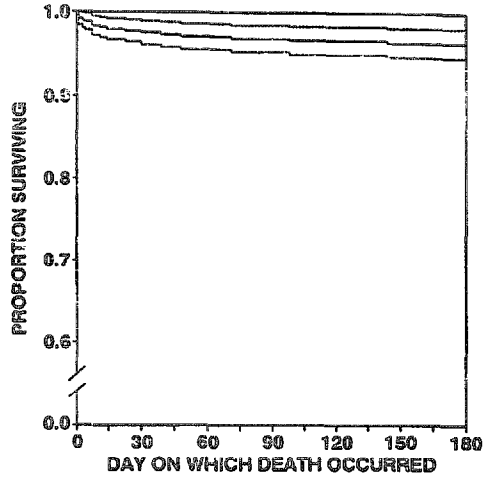

Figure 3. Kaplan-Meier curve for survival in the 6-month period after stenting for acute or threatened vessel closure. Upper and lower curves represent the 95% confidence interval.

63 ± 25% before stenting to 15 ± 14% after stenting. The improvement was from 75 ± 31% to 16 ± 16% in the group with acute vessel closure and from 58 ± 20% to 14 ± 13% in the threatened closure group.

Deployment problems. In 24 (4.6%) of the patients in whom stent placement was attempted, no stent was placed. The reasons for not deploying stents were related to either the device (6 patients) or to coronary anatomy (18 patients). Device-related problems tended to occur early in the study and may be attributable to lack of experience with the device. They included inability to cross the hub of the guiding catheter with the stent/balloon catheter and inadequate guide wire and guiding catheter support. Anatomy-related factors included inability to reach the lesion (usually because of severe tortuosity of the vessel proximal to the site of intended stent placement) and inability to cross the lesion with the stent/balloon catheter. Inability to reach the lesion with the device accounted for nine patients not receiving stents and inability to cross the lesion prevented stenting in another nine. The undeployed stents were all successfully withdrawn from these patients.

Clinical outcome after stenting. In-hospital clinical success (that is, angiographic success with no death, bypass graft surgery or myocardial infarction) was achieved in 420 (87.3%) of the 481 patients with angiographic success. Table 3A presents the incidence of death, bypass surgery and myocardial infarction during the in-hospital period immediately after stent placement and before hospital discharge. Results are presented for the acute closure and threatened vessel closure groups separately and combined. The in-hospital mortality rate was 2.2% (2.6% for patients with acute closure and 2.1% for patients with threatened closure). In-hospital myocardial infarction, including those events related to the initial angioplasty complication, occurred in 5.5% of patients (7.6% with acute closure and 4.3% with threatened closure). A Q wave myocardial infarction occurred in 3% of patients (3.8% with acute closure and 2.7% with threatened closure). Emergency bypass graft surgery was required in 4.3% of patients (7.7% with acute closure and 2.7% with threatened closure). As expected, the incidence of adverse events was slightly higher in the acute closure group, but the difference was significant only for emergency bypass surgery ($p = 0.021$).

During the 6-month period after discharge from stent placement, the incidence of death and myocardial infarction was similar in the acute and threatened closure groups, whereas bypass surgery was slightly but not significantly more common in the threatened closure group. The timing of these events varied during the 6-month follow-up period (Fig. 3 to 5). The majority of the deaths in this period occurred within 30 days of stenting and the probability of surviving 6 months was approximately 97% (Fig. 3). The probability of surviving 6 months without requiring bypass surgery was approximately 85% (Fig. 4). Most bypass surgery was performed electively because of lesion restenosis after 2 to 3 months. Finally, the incidence of myocardial infarction was low and occurred mainly within the 1st month (Fig. 5). The probability of surviving 6 months with no myocardial infarction was approximately 93%.

Angiographic follow-up. Of this study cohort, 384 patients were available for follow-up angiography, surviving ≥4 months after the angioplasty/stent procedure with no need for bypass surgery or other complications that would preclude repeat catheterization. Follow-up angiography was performed in 336 (87.5%) of these 384 patients. Of the remaining 48 patients, 43 (11.2%) refused to undergo repeat

JACC Vol. 22, No. 1
July 1993:135–43

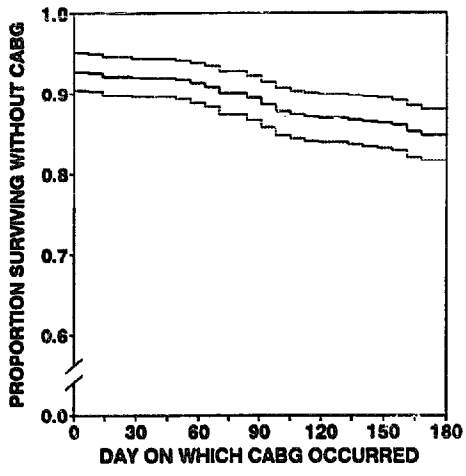

Figure 4. Kaplan-Meier curve for the incidence of coronary artery bypass surgery (CABG) in the 6-month period after stenting for acute or threatened vessel closure. **Upper and lower curves** represent the 95% confidence interval.

catheterization; 4 patients (1%) undergoing early recatheterization had repeat angioplasty of the stented region and are waiting an additional 6 months for follow-up evaluation and 1 additional patient has not yet had follow-up catheterization.

For the entire group of patients undergoing 6-month angiographic follow-up study, the percent diameter stenosis averaged 46 ± 31% (48 ± 29% for the acute closure group [n = 108] and 45 ± 31% for the threatened closure group [n = 228]). The incidence of restenosis, defined as >50% diameter stenosis at follow-up study, was 38% for the acute closure group (41 of 108) and 39.5% for the threatened closure group (90 of 228). Overall, the incidence of restenosis was 39%. Repeat angioplasty was performed in 42

Figure 5. Kaplan-Meier curve for the incidence of myocardial infarction (MI) in the 6-month period after stenting for acute or threatened vessel closure. **Upper and lower curves** represent the 95% confidence interval.

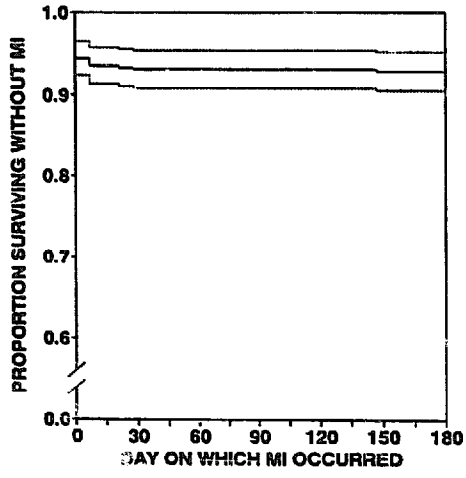

Table 4. Blood Loss Complications Requiring Transfusion

Blood Loss Site	Patients (no.)
Arterial access site*	57
Gastrointestinal	9
Depressed hemoglobin	7
Retroperitoneum	4
Hematuria	2
Hemorrhagic cystitis	2
Intracranial	1
Soft tissue	1
Total	83

*Subsequently, three of these patients also had episodes of gastrointestinal bleeding and one had intracranial bleeding.

patients (8.5%) within 6 months of the angioplasty/stent procedure.

The influence of stent diameter on the incidence of restenosis in patients having 6-month follow-up angiography was evaluated by nonparametric chi-square analysis. Restenosis of the stented artery was reported in 35% (7 of 20 patients) with 4-mm diameter stents, 25% (13 of 52 patients) with 3.5-mm stents, 45.7% (63 of 138 patients) with 3-mm stents, 38.1% (45 of 118 patients) with 2.5-mm stents and 37.5% (3 of 8 patients) with 2-mm stents. Chi-square analysis of these results indicated that restenosis was independent of stent diameter ($\chi^2 = 4.29$, $< \chi^2_{0.05(4)} = 9.49$).

The implantation of multiple stents during a single procedure was not associated with an increased restenosis rate. Twelve (40%) of 30 patients receiving two or more stents during a single procedure exhibited restenosis of the stented artery compared with 120 (39.2%) of 306 patients receiving a single stent. Chi-square analysis showed these rates to be not significantly different.

Complications. The incidence of bypass surgery, myocardial infarction and death has already been discussed with regard to clinical outcome. Other complications included blood loss requiring transfusion and subacute thrombosis at the stent site.

Eighty-three patients (16.8%) required transfusions after the angioplasty/stenting procedure. Table 4 presents a stratification of the reasons given for requiring transfusion. Blood loss from the arterial access site accounted for 69% (57 of 83) of the reported bleeding complications. Four retroperitoneal hematomas were reported. Primary gastrointestinal blood loss was reported in nine patients and was the second most frequent reason for transfusion, followed by depressed hemoglobin in seven patients. The incidence of blood loss requiring transfusion decreased throughout the study, especially once the value of gradual mobilization was identified. Before March 1990, the incidence of blood loss requiring transfusion was 24.6% (29 of 118 bleeding complications). At that time, the importance of graduated mobilization was reported at an investigators' meeting and incorporated into the poststenting protocol. Since then, the bleeding complication rate has decreased to 14.4% (54 of 376 bleeding complications) and continues to improve.

Thrombosis of the stented artery was reported in 43 patients (8.7%) after stent placement. In 17 of these patients, thrombus was reported present before stent implantation. Thrombosis in these patients occurred an average of 5.2 ± 6.2 (range 0 to 29) days after stenting. Twenty-five of the 43 patients had the region reopened by angioplasty or lytic therapy. One of these 25 patients had emergency coronary artery bypass graft surgery and two had nonemergency bypass surgery (at 4 and 13 days after stenting). Eleven of these 25 patients had a myocardial infarction (Q wave in 6 and non-Q wave in 5). Eighteen of the 43 patients did not have the occluded region reopened. Three of these patients had emergency coronary artery bypass graft surgery and six had nonemergency bypass surgery (at 2, 2, 3, 4, 4 and 5 days after stenting, respectively). Three of these 18 patients had late coronary artery bypass graft surgery (at 17, 29 and 71 days after stenting, respectively). Nine of the 18 patients were reported to have myocardial infarction (Q wave in 6 and non-Q wave in 3). Two of the 18 patients died in the hospital (at 3 and 7 days, respectively, after stenting). The incidence of thrombosis has decreased over the course of the study. The thrombosis rate was 11.9% (14 of 118 patients) in the initial reporting period (September 1988 to March 1990), 10.9% (19 of 174 patients) in the period from March 1990 to September 1990 and 5% (10 of 202 patients) from September 1990 through June 1991.

The influence of stent diameter on the incidence of thrombosis of the stented artery was evaluated by nonparametric chi-square analysis. Thrombosis of the stented artery was reported in none of the 25 patients with 4-mm diameter stents, 11.4% (8 of 70 patients) with 3.5-mm stents, 7.6% (16 of 210 patients) with 3-mm stents, 8.7% (15 of 173 patients) with 2.5-mm stents and 25% (4 of 16 patients) with 2-mm stents. Chi-square analysis of these results indicated that thrombosis was independent of stent diameter ($\chi^2 = 8.26$, $< \chi^2_{0.05(4)} = 9.49$). However, because of the small number of patients receiving 2-mm stents, the addition of a single patient with thrombosis in the 2-mm group would make the incidence significant.

The implantation of multiple stents during a single procedure was not associated with an increased incidence of stent thrombosis. Three (6.7%) of 45 patients receiving two or more stents during a single procedure exhibited thrombosis of the stented artery compared with 40 (8.9%) of 449 patients receiving a single stent. These rates were not significantly different by chi-square analysis.

Discussion

Present study. This early multicenter series of patients receiving a coronary stent for acute or threatened vessel closure represents the learning curve experience with the first clinically available prototype of the device. The series includes subjects treated during a time when correct patient selection criteria and management strategies were being developed. It also includes a large proportion of investigative sites and investigators with relatively limited experience with the device. Accordingly, the results of this study should represent those that might be expected when the device is used in clinical practice provided the correct patient management protocols are followed.

Despite the limitations of the learning curve experience, the stent was deployed and improved blood flow in >95% of patients. The initial success rate ranged from 92.6% to 100% in centers treating ≥20 patients. The stent could not be placed in <5% of the patients in whom the procedure was attempted. Failure to place stents was due to a variety of factors, including operator inexperience, complex anatomy and inadequate guide support. In addition, patient selection improved as the limitations of the device emerged. Extensive dissections extending far distally into the vessel were found to be unsuitable for stenting, as were vessels with poor distal "runoff" and severely tortuous and calcified vessels.

Overall, the device appears to offer a satisfactory nonsurgical solution to the problem of acute closure or vessel dissection complicating coronary interventions. Emergency bypass surgery was required in only 4.3% of these patients and the total incidence of in-hospital surgery was 7.3%. There was a wide variation in the need for bypass graft surgery among centers, ranging from 0% to 11% at centers where ≥20 patients underwent stenting. Similarly, the low incidence of in-hospital Q wave myocardial infarction (3%) suggests a favorable benefit from this approach. Moreover, the decrease in the incidence of both thrombosis of the stented vessel and bleeding complications over the course of the study indicates that these potential complications are manageable with rigorous monitoring of the anticoagulant regimen and graduated ambulation.

It is not possible from this study to determine the overall clinical benefit associated with the use of this device. However, despite learning curve problems, the incidence of emergency surgery and myocardial infarction observed in this study compares favorably with that reported in previous series (1–4) of acute vessel closure after coronary angioplasty. These previous clinical investigations reported the need for in-hospital coronary bypass graft surgery in 33% to 40.6% of cases and an incidence of myocardial infarction ranging from 28% to 53.8%. The device should be viewed only as an adjunct to currently available methods used to solve the problems of unsatisfactory results after coronary intervention. Prolonged balloon inflations represent first-line therapy for acute or threatened closure, with stenting being a second-line therapy only in those patients without clinical and anatomic contraindications to stent placement. For some patients, alternative therapy such as bypass graft surgery or conservative medical management represents the preferred approach.

Hemorrhagic complications. Because all patients require carefully managed anticoagulant protocols after stenting, hemorrhagic complications are not uncommon. Approximately 17% of patients in this series required a blood transfusion after the angioplasty/stenting procedure, al-

JACC Vol. 22, No. 1
July 1993:135–43

though some of the blood loss was associated with a complex and prolonged angioplasty procedure and most (69%) of the bleeding complications involved the femoral artery puncture site. Gastrointestinal bleeding requiring transfusion occurred in 1.8% of patients, retroperitoneal hemorrhage in 0.8% and an intracranial hemorrhage in 0.2% (one patient). Although hemorrhagic complications were a significant problem, there was a wide institutional variation in the incidence of hemorrhagic events, ranging from 0% to 32% in centers performing the procedure in ≥20 patients, and a learning curve effect evidenced by a marked reduction in bleeding complications over time. Several factors probably played a role in this improvement, including better patient selection, the use of prolonged C-clamp compression on the femoral puncture site, moderating the level of anticoagulation and initiating 72 h of bed rest after the procedure. Hemorrhagic problems may be further reduced in the future through the use of better femoral puncture closure techniques and the use of less thrombogenic stents that will facilitate less aggressive anticoagulant regimens.

Thrombosis of the stented artery occurred in 8.7% of patients in this series. This complication was responsible for myocardial infarction in 4% of patients and referral for bypass in 3%. In >50% of the patients with stent thrombosis, the vessel could be reopened with repeat angioplasty or thrombolytic therapy. The incidence of stent thrombosis also decreased over time and varied greatly among centers, ranging from 0% to 15.2% in centers treating ≥20 patients. Thrombosis occurred an average of 5.2 ± 6.2 days (range 0 to 29) after stenting, in some instances shortly after discontinuation of heparin. Appropriate patient selection, stenting technique and vigilant management of the antiplatelet and anticoagulant regimen appear to be important in avoiding stent thrombosis. Of particular importance is the presence of residual or uncovered dissection and the placement of stents in vessels with preexisting untreated thrombus or poor distal runoff. Forty percent of the stents with subacute thrombosis had angiographically evident thrombus in the vessel before stenting. Prolonged (12 to 24 h) intracoronary side-hole delivery of urokinase may be used as an adjunct to stenting in such patients.

The incidence of thrombosis was statistically independent of the stent diameter. However, for the 2-mm stents, this result was borderline. That is, if one additional patient with a 2-mm stent had exhibited thrombosis, the result would have been significant. Thus, the 25% incidence of thrombosis in patients receiving 2-mm stents warrants caution when use of this size stent is contemplated. The implantation of multiple stents was not associated with an increase in thrombosis in the stented vessel.

Restenosis. Despite favorable initial angiographic and clinical results, 39% of patients undergoing follow-up recatheterization showed evidence of restenosis defined as >50% diameter narrowing. However, in the critical situation of acute or threatened closure, the primary value of the coronary stent is its ability to provide a rapidly applied nonsurgical alternative to correct or prevent the abrupt closure of a coronary artery after an unsuccessful angioplasty procedure, not its ability to prevent restenosis. Late cardiac death or myocardial infarction was uncommon. The restenosis rate was not influenced by the diameter of the stent used or by the implantation of multiple stents. The restenosis phenomenon after stenting for acute or threatened vessel closure with this device appears to follow a similar pattern to that seen after routine elective balloon angioplasty. Most patients who required further revascularization could be managed by repeat balloon dilation. Although the restenosis rate appears high, the patients included in this study had complex lesion morphology that predisposed to coronary dissection. Similar cohorts of patients who could be managed by repeat angioplasty alone have been reported to have restenosis rates of >55% (16).

Limitations to the study. There are several limitations to this study. This study was not designed as a randomized trial. When the study began, the only viable alternative to stenting for acute vessel closure was emergency bypass surgery. Because the need for bypass surgery was considered an adverse outcome of the stenting procedure, appropriate comparisons between a group of patients with stenting and a group of patients undergoing emergency bypass surgery were not possible. Because prolonged balloon inflation was not considered a standard alternative treatment when this study began, such patients were not acceptable as a control group. The study may have been limited by changes in clinical practice, the increasing complexity of lesions accepted for angioplasty, improved angioplasty balloon technology and techniques and alternative therapies not available at the beginning of the study. Nevertheless, the measured end points were reasonably hard (namely, the incidence of myocardial infarction, coronary artery bypass graft surgery and death) and comparisons are possible with previous reports of similar patients with periprocedural occlusion associated with coronary angioplasty.

Conclusions. This early multicenter experience suggests that this stent is a useful adjunct percutaneous intervention to prevent or minimize complications associated with flow-limiting coronary artery dissections that cannot be corrected with conventional percutaneous techniques. Although this study was not randomized, it demonstrates a high technical success rate and encouraging results with respect to the low incidence of emergency coronary artery bypass surgery and myocardial infarction.

We acknowledge the contributions of David Hall, MD, George Rodgers, MD, Gerald Dorros, MD, Morton Kern, MD, Richard Stack, MD, Tim Fischell, MD, Ronald Vlietstra, MD, James Margolis, MD, Jerome Segal, MD and Tomoaki Hinohara, MD in enrolling patients into this clinical investigation. We are grateful for the efforts of the research coordinators at each institution in the timely preparation and submission of case reports and, in particular, for their commitment to patient care. We also thank Sharon Cicardo and Serena Kibler of MED Institute, Inc., for their dedication to coordinating data collection, entry and validation.

Appendix

Investigative Centers and Principal Investigators

Emory University Hospital, Atlanta, GA: Spencer B. King (100*).
University of Alabama at Birmingham, Birmingham, AL: Gary S. Roubin (95).
St. Vincent's Hospital, Indianapolis, IN: Cass A. Pinkerton (82).
Riverside Methodist Hospital, Columbus, OH: Barry S. George (59).
The Methodist Hospital, Houston, TX: Albert E. Raizner (33).
Mayo Clinic, Rochester, MN: David R. Holmes (29).
University of Michigan Medical Center, Ann Arbor, MI: Eric J. Topol (25).
The Christ Hospital, Cincinnati, OH: Dean J. Kereiakes (20).
St. Luke's Hospital of Kansas City, Kansas City, MO: Geoffrey O. Hartzler (10).
St. Thomas Medical Center, Nashville, TN: David Hall (9).
St. David's Hospital, Austin, TX: George P. Rodgers (7).
St. Luke's Hospital, Milwaukee, WI: Gerald Dorros (7).
St. Louis University Medical Center, St. Louis, MO: Morton J. Kern (6).
Duke University Medical Center, Durham, NC: Richard S. Stack (4).
Stanford University Medical Center, Stanford, CA: Tim A. Fischell (2).
Watson Clinic, Lakeland, FL: Ronald E. Vlietstra (2).
Miami Heart Institute, Miami Beach, FL: James R. Margolis (2).
George Washington Medical Center, Washington, D.C.: Jerome Segal (1).
Sequoia Hospital, Redwood, CA: Tomoaki Hinohara (1).

*Figures in parentheses indicate the number of patients treated with stenting at each institution.

References

1. Detre KM, Holmes DR, Holubkov R, et al. Incidence and consequences of periprocedural occlusion: the 1985–1986 National Heart, Lung, and Blood Institute Percutaneous Transluminal Coronary Angioplasty Registry. Circulation 1990;82:739–50.
2. Simpfendorfer C, Belardi J, Bellamy G, Galan K, Franco I, Hollman J. Frequency, management and follow-up of patients with acute occlusion after percutaneous transluminal coronary angioplasty. Am J Cardiol 1987;59:267–9.
3. Ellis SG, Roubin GS, King SB, et al. Angiographic and clinical predictors of acute closure after native vessel coronary angioplasty. Circulation 1988;77:372–9.
4. Sinclair IN, McCabe CH, Sipperly ME, Baim DS. Predictors, therapeutic options and long-term outcome of abrupt reclosure. Am J Cardiol 1988;61:61G–6G.
5. Sigwart U, Puel J, Mirkovitch V, Joffre F, Kappenberger L. Intravascular stents to prevent occlusion and restenosis after transluminal angioplasty. *N Engl J Med 1987;316:701–6.*
6. Serruys PW, Strauss BH, Beatt KJ, et al. Angiographic follow-up after placement of a self-expanding coronary-artery stent. N Engl J Med 1991;324:13–7.
7. Schatz RA, Baim DS, Leon M, et al. Clinical experience with the Palmaz-Schatz coronary stent: initial results of a multicenter study. Circulation 1991;83:148–61.
8. Roubin GS, Robinson KA, King SB, et al. Early and late results of intracoronary arterial stenting after coronary angioplasty in dogs. Circulation 1987;76:891–7.
9. Robinson KA, Roubin GS, Siegel RJ, Black AJ, Apkarian RP, King SB. Intra-arterial stenting in the atherosclerotic rabbit. Circulation 1988;78: 646–53.
10. Rodgers GP, Minor ST, Robinson K, et al. Adjuvant therapy for intracoronary stents: investigations in atherosclerotic swine. Circulation 1990; 82:560–9.
11. Albert E. Raizner, Minor ST, Siegel CO, et al. Dimensional stability of the Gianturco-Roubin balloon expandable stent assessed by quantitative coronary angiography (abstr). J Am Coll Cardiol 1991;17:301A.
12. Garratt KN, Holmes DR, Roubin GS. Early outcome after placement of a metallic intracoronary stent: initial Mayo Clinic experience. Mayo Clin Proc 1991;66:268–75.
13. Roubin GS, Cannon AD, Agrawal SK, et al. Intracoronary stenting for acute and threatened closure complicating percutaneous transluminal angioplasty. Circulation 1992;85:916–27.
14. Anderson PG, Bajaj RK, Baxley WA, Roubin GS. Vascular pathology of balloon expandable flexible coil stents in humans. J Am Coll Cardiol 1992;19:372–81.
15. Roubin GS. Trials and tribulations in the development of the coronary artery stent: a personal perspective. J Invasive Cardiol 1992;4:69–74.
16. Ba'albaki HA, Weintraub WS, Tao X, et al. Restenosis after acute closure and successful reopening: implications for new devices (abstr). Circulation 1990;82(suppl III):III-314.